

Sulfisomidine in the Treatment of Pertussis

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ALTHOUGH wide-spectrum antibiotics have been widely used in the treatment of pertussis, few reports have appeared in the literature on the use of sulfonamides for this purpose. A laboratory study by Bradford, Brooks and Katsampes¹ showed that sulfonamides may have a specific action against experimental pertussis. They administered sulfadiazine and immune rabbit serum separately to mice infected with murine pertussis and found that each protected the animals when given 24 hours after infection.

Brainerd² reported upon a clinical study in which a sulfonamide was used for whooping cough. He administered sulfadiazine and hyperimmune gamma globulin to a group of 26 infants who had pertussis complicated by pneumonia, many of whom appeared almost moribund when first seen. In another group, 26 infants with uncomplicated pertussis, only nine of whom were febrile, were treated with hyperimmune gamma globulin alone. It was observed that the latter treatment "appeared to shorten the course, lessen the severity and reduce the rate of complications"; but the combination of sulfadiazine with hyperimmune gamma globulin had added merit in that it "appeared to affect favorably the mortality rate of pertussis complicated by pneumonia."

In view of the limited number of reported studies in this field, the authors observed a group of 21 patients with pertussis who were treated with sulfisomidine (Elkosin®) in the Communicable Disease Unit of the Los Angeles County Hospital. Sulfisomidine replaced chloramphenicol as the drug used in the treatment of whooping cough. However, hyperimmune pertussis serum was continued in the same manner as with the previous regimen.

The patients in this study varied in ages, the extremes being seven weeks and five years. Fourteen of the patients were females and seven were males. Seven of the cases were complicated by bronchopneumonia. The average time in the hospital was ten days; the shortest stay was five days and the longest 25 days. There were no deaths in this series.

The dose of sulfisomidine used was 0.26 gm. per kilogram of body weight per 24 hours. It was given

• Sulfisomidine and pertussis serum were used in the treatment of 21 patients with pertussis. Twenty of the patients were under six months of age and seven had bronchopneumonia.

Therapeutic concentrations of the drug in the blood were obtained in 14 cases when it was given in dosage of 0.26 gm. per kilogram of body weight per 24 hours.

The average stay in hospital was ten days. None of the patients died. Hematuria developed in one case but crystalluria was not concomitant and it abated promptly when fluid intake was increased.

orally. No alkalinizing solutions or other drugs were given. Administration of the drug was started as soon as examinations of the blood and urine at the time of admittance were completed. The content of sulfisomidine in the blood and urine was determined for the first time 24 to 36 hours after the initial dose of the drug. Subsequent determinations were done at 24 to 72-hour intervals during the period of administration.

Therapeutic concentrations in the blood—more than 10.0 mg. per 100 cc.—were achieved in 16 of the cases in 36 hours after the start of treatment. These levels were easily maintained on a standard maintenance dose. Sulfisomidine was rapidly excreted in the urine. The simultaneous determinations of content in the blood and the urine showed a highly variable ratio without value in attempted correlation. Hemolytic anemia or agranulocytosis did not develop in any of these cases.

As to blood concentrations of the drug, the lowest was 5.0 mg. per 100 cc. (two cases) and the highest 53.1 mg. per 100 cc. (one case). In five patients the concentration was between 5.0 and 10.0 mg. per 100 cc., in seven between 10.0 and 20.0 mg., in three between 20.0 and 30.0 mg., and in six it was greater than 30.0 mg. per 100 cc.

Concentrations in the urine, in milligrams per 100 cc., were as follows: 2.8 to 10.0, three patients; 10.0 to 20.0, two patients; 20.0 to 30.0, one patient; greater than 30.0, twelve patients. The highest concentration in the urine was 113.0 mg. per 100 cc.

Only one patient in the series had hematuria. This developed on the seventh day of therapy when the blood level was 12.9 mg. of sulfisomidine per 100 cc. and the urine level was 40 mg. per 100 cc. The urine pH was 5. At the time, the reaction for

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albumin was 1 plus, but there was no crystalluria in spite of the acid urine. Hematuria abated promptly when fluid intake was increased. Repeated urinalysis on all the patients revealed acid urine and without exception the pH never was greater than 5. In spite of this, no sulfonamide crystals or red blood cells were ever found in the urine.

The highest blood level of sulfisomidine in any case in the series (53.1 mg. per 100 cc.) was concomitant with a level of 59.3 mg. per 100 cc. of urine. The patient was a girl three and a half months of age who was in an excellent state of hydration and nutrition at the start of therapy. This patient had been ill for seven days prior to admission to the hospital. Cyanosis associated with paroxysmal coughing was noted for the first time on the day of admission. The infant received 250 mg. of sulfisomidine by mouth at the time of admission and every six hours thereafter. In addition 5 cc. of pertussis serum was given intramuscularly, along with other supportive measures. Approximately 36 hours after the first dose of sulfisomidine the blood level was 23.5 mg. per 100 cc., seventy-two hours later the blood content was 53.1 mg. and the urine content was 59.3 mg. per 100 cc.

It is of interest to note that for the year between July 1, 1952, and June 30, 1953, a total of 244 patients were treated for pertussis in the Communicable Disease Unit of the Los Angeles County Hospital. Excluding the 21 patients reported upon here, 25 (11.2 per cent) had bronchopneumonia and four patients (1.7 per cent) died. Only 42 per cent of the 233 patients were less than six months of age, and 22.4 per cent were under three months. Of the 21 patients in the present study, 20 (96 per cent) were less than six months of age and seven (33.8 per cent) were under three months. In one-third of

the patients under six months of age the disease was complicated with bronchopneumonia. There were no deaths in the present study group.

A comparison cannot properly be made between the larger group (223 cases) treated with pertussis serum and chloramphenicol, and the small group of 21 patients treated with hyperimmune pertussis serum and sulfisomidine. However, if it be conceded that, regardless of therapy, the death rate is highest in patients from one month to six months of age, then this study—96 per cent of the patients in this very young age group and no deaths in the small series, as compared with the 33 per cent in that age group in the larger series, with four deaths—would suggest that sulfisomidine is very effective in the treatment of pertussis.

CONCLUSIONS

Sulfisomidine is a relatively safe and effective chemotherapeutic agent in the treatment of pertussis. High blood concentrations of the drug are readily obtained when it is given orally. It is excreted rapidly in the urine. Alkalinization appears unimportant inasmuch as in this study acidity of the urine did not significantly precipitate untoward or toxic reactions as long as hydration was adequate.

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